#### **REMARKS**

#### 1. Introduction

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and the reasons that follow.

Claims 105, 107, 115 and 117 are amended, and claims 146 and 147 are added. Support for these amendments can be found, *inter alia*, on pages 30-34 of the specification, and in the Examples and original claims.

Úpon entry of these Amendments, claims 105-147 will be pending. These claims are presented for reconsideration.

## 2. Response to Issues Raised by Examiner in Outstanding Office Action

## a. Claim Rejections - 35 U.S.C. § 102

Claims 105-145 were rejected under 35 U.S.C. § 102(e) as being allegedly anticipated by Krishnamurthy (U.S. Pat. No. 6,399,314). Applicants respectfully traverse this rejection.

The instant claims recite peptide probes comprising an amino acid sequence corresponding to a  $\beta$ -sheet forming region of a target protein, wherein the peptide probe exhibits a random coil or alpha-helix conformation in solution, and undergoes a transition to a  $\beta$ -sheet conformation upon interaction with misfolded target protein exhibiting a  $\beta$ -sheet conformation, and wherein at least 75% of the amino acid residues are hydrophobic amino acids. Such probes are not taught or suggested by Krishnamurthy.

Krishnamurthy was cited for allegedly teaching "detection of aggregated forms of amyloid peptide using amyloid-specific spectroscopic probes." Office Action, page 2. Krishnamurthy is primarily directed to the use of spectroscopic dyes such as Congo red for the detection of aggregated amyloid protein; however, it does mention that "fluorophore-labeled amyloid peptides" can be used. While the Examiner cites Krishnamurthy's statement that the amyloid peptides can be portions of amyloid polypeptides capable of co-aggregating with amyloid polypeptides, the Examiner should recognize that there is no teaching in

Krishnamurthy of any specific peptides that may be useful, and no guidance provided as to which "portions" of an amyloid peptide might be useful. Thus, Krishnamurthy plainly fails to teach or suggest the probes recited in the instant claims. For example, Krishnamurthy does not teach a probe with an amino acid sequence corresponding to a β-sheet forming region of a target protein that comprises 75% hydrophobic amino acid residues. (Proteins generally do not comprise 75% hydrophobic residues; thus, a random selection of amyloid proteins or portions thereof would not result in polypeptides comprising 75% hydrophobic amino acid residues.) Because Krishnamurthy does not teach or suggest the probes recited in the instant claims, the §102 rejection is improper and should be withdrawn.

The Office Action fails to show how Krishnamurthy anticipates the dependent claims, and indeed it does not. For example, there is no teaching or suggestion in Krishnamurthy of a peptide comprising two amino acid sequences corresponding to a β-sheet forming region of a target protein (recited, e.g., in claim 112 and its dependents), of a peptide comprising two amino acid sequences oriented in a palindromic fashion (recited, e.g., in claims 113-114), of peptides labeled at both termini (recited, e.g., in claims 123 and 147), or of peptide probes that consist of 10 to 25 residues, or of methods of using such peptides. Thus, the §102 rejection of these claims is improper, and should be withdrawn.

# b. Obviousness-Type Double Patenting

Claims 105 and 125 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 7,166,471. Without acquiescing to this rejection, and solely to advance prosecution, a terminal disclaimer over U.S. Pat. No. 7,166,471 is submitted herewith. Accordingly, this rejection is moot.

### **CONCLUSION**

The application is believed to be in condition for allowance, and an early notice to that effect is earnestly solicited.

Should there be any questions regarding this submission, or should any issue remain, the Examiner is invited to contact the undersigned in order to advance prosecution.

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The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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